

WHAT IS CLAIMED IS:

1. A method for inactivating a virus in a patient comprising administering to said patient a modified siRNA in an effective amount to inactivate said virus.
2. The method of claim 1, wherein said modified siRNA is a 2' modified siRNA.
3. The method of claim 2, wherein the modification is at the 2' position of at least one ribonucleotide of said siRNA.
4. The method of claim 3, wherein said modification is selected from the group consisting of fluoro-, methyl-, methoxyethyl- and propyl-modification.
5. The method of claim 4, wherein said fluoro-modification is a 2'-fluoro-modification or a 2',2'-fluoro-modification.
6. The method of claim 5, wherein pyrimidines of said siRNA are modified, and said pyrimidines are cytosine, a derivative of cytosine, uracil, a derivative of uracil or a combination thereof.
7. The method of claim 1, wherein both strands of said siRNA contain at least one modified nucleotide.
8. The method of claim 1, wherein said virus is selected from the group consisting of hepatitis C virus (HCV), hepatitis A virus, hepatitis B virus, hepatitis D virus, hepatitis E virus, Ebola virus, influenza virus, rotavirus, reovirus, retrovirus, poliovirus, human papilloma virus (HPV), metapneumovirus and coronavirus.
9. The method of claim 8, wherein said virus is hepatitis C virus.
10. The method of claim 8, wherein said siRNA is prepared by

(a) identifying a target nucleotide sequence in an HCV genome for designing a small interfering RNA (siRNA); and

(b) producing an siRNA that has been modified to contain at least one modified nucleotide.

11. The method of claim 8, wherein said siRNA is prepared by

(a) identifying a target nucleotide sequence in a virus genome for designing a small interfering RNA (siRNA); and

(b) producing an siRNA that has been modified to contain at least one modified nucleotide.

12. The method of claim 10, wherein said target nucleotide sequence is selected from the group consisting of 5'-untranslated region (5'-UTR), 3'-untranslated region (3'-UTR), core, and NS3 helicase.

13. The method of claim 12, wherein said siRNA is siRNA5, siRNAC1, siRNAC2, siRNA5B1, siRNA5B2 or siRNA5B4.

14. An siRNA comprising a modified ribonucleotide, wherein said siRNA is resistant to RNase and retains the ability to inhibit viral replication.

15. The siRNA of claim 14, wherein said modified siRNA is a 2' modified siRNA.

16. The siRNA of claim 15, wherein the modification is at the 2' position of at least one ribonucleotide of said siRNA.

17. The siRNA of claim 14, wherein the modification is selected from the group consisting of fluoro-, methyl-, methoxyethyl- and propyl-modification.
18. The siRNA of claim 17, wherein said fluoro-modification is a 2'-fluoro-modification or a 2',2'-fluoro-modification.
19. The method of claim 18, wherein pyrimidines of said siRNA are modified, and said pyrimidines are cytosine, a derivative of cytosine, uracil, a derivative of uracil or a combination thereof.
20. The siRNA of claim 14, wherein both strands of the siRNA contains modified nucleotides.
21. The siRNA of claim 14, wherein said siRNA interacts with a target nucleotide sequence in a virus genome.
22. The siRNA of claim 21, wherein said virus is selected from the group consisting of hepatitis C virus (HCV), hepatitis A virus, hepatitis B virus, hepatitis D virus, hepatitis E virus, Ebola virus, influenza virus, rotavirus, reovirus, retrovirus, poliovirus, human papilloma virus (HPV), metapneumovirus and coronavirus.
23. The siRNA of claim 22, wherein said virus is hepatitis C virus (HCV).
24. A method of making a modified siRNA that targets a nucleic acid sequence in a virus comprising:
  - (a) preparing a modified-double stranded RNA (dsRNA) fragment containing at least one modified ribonucleotide in at least one strand that spans the genome of a target agent; and

(b) cleaving said modified-dsRNA fragments with recombinant human Dicer resulting in more than one modified siRNA.

25. The method of claim 24, further comprising:  
(c) isolating said modified siRNAs.

26. The method of claim 24, wherein said target agent is a virus.

27. The method of claim 26, wherein said virus is selected from the group consisting of hepatitis C virus (HCV), hepatitis A virus, hepatitis B virus, hepatitis D virus, hepatitis E virus, Ebola virus, influenza virus, rotavirus, reovirus, retrovirus, poliovirus, human papilloma virus (HPV), metapneumovirus and coronavirus.

28. A method for inactivating a virus in a patient comprising administering to said patient a modified siRNA consisting of about 10 to about 30 ribonucleotides in an effective amount to inactivate said virus.

29. The method of claim 28, wherein said modified siRNA consists of about 19 to about 23 ribonucleotides.

30. The method of claim 28, wherein said modified siRNA is a 2' modified siRNA.

31. The method of claim 30, wherein the modification is at the 2' position of at least one ribonucleotide of said siRNA.

32. The method of claim 31, wherein said modification is selected from the group consisting of fluoro-, methyl-, methoxyethyl- and propyl-modification.

33. The method of claim 32, wherein said fluoro-modification is a 2'-fluoro-modification or a 2',2'-fluoro-modification.

34. The method of claim 28, wherein pyrimidines of said siRNA are modified and said pyrimidines are cytosine, a derivative of cytosine, uracil, a derivative of uracil or a combination thereof.

35. The method of claim 28, wherein both strands of said siRNA contain modified nucleotides.

36. The method of claim 28, wherein said virus is selected from the group consisting of hepatitis C virus (HCV), hepatitis A virus, hepatitis B virus, hepatitis D virus, hepatitis E virus, Ebola virus, influenza virus, rotavirus, reovirus, retrovirus, poliovirus, human papilloma virus (HPV), metapneumovirus and coronavirus.

37. The method of claim 36, wherein said virus is hepatitis C virus (HCV).

38. The method of claim 37, wherein said siRNA is prepared by

(a) identifying a target nucleotide sequence in a HCV genome for designing a small interfering RNA (siRNA); and

(b) producing an siRNA that has been modified to contain at least one modified nucleotide.

39. The method of claim 36, wherein said siRNA is prepared by

(a) identifying a target nucleotide sequence in a virus genome for designing a small interfering RNA (siRNA); and

(b) producing an siRNA that has been modified to contain at least one modified nucleotide.

40. The method of claim 38, wherein said target nucleotide sequence comprises a conserved nucleotide sequence necessary for HCV replication.
41. The method of claim 40, wherein said conserved nucleotide sequence is selected from the group consisting of 5'-untranslated region (5'-UTR), 3'-untranslated region (3'-UTR), core, and NS3 helicase.
42. The method of claim 41, wherein said siRNA is siRNA5, siRNAC1, siRNAC2, siRNA5B1, siRNA5B2 or siRNA5B4.
43. A double-stranded RNA molecule of from about 10 to about 30 nucleotides that inhibits replication of hepatitis C virus (HCV).
44. The double-stranded RNA molecule of claim 43 comprising a nucleotide sequence at least 80% identical to the nucleotide sequence of siRNA5, siRNAC1, siRNAC2, siRNA5B1, siRNA5B2 or siRNA5B4.
45. A method of inducing targeted RNA interference toward HCV in hepatic cells, comprising administering the double-stranded RNA molecule of claim 43 to hepatic cells, wherein the nucleotide sequence of said double-stranded RNA molecule corresponds to an HCV nucleotide sequence.
46. A method of inhibiting replication of hepatitis C virus (HCV), comprising administering the RNA polynucleotide molecule of claim 44 to cells infected with HCV.
47. A vector comprising a DNA segment encoding the RNA molecule of claim 43.

48. The vector of claim 47, wherein the sense strand of said double-stranded RNA molecule is operably linked to a first promoter and wherein the antisense strand of said double-stranded RNA molecule of is operably linked to a second promoter.

49. The vector of claim 48, wherein said first and second promoters are selected from the group consisting of U6 and H1.

50. The vector of claim 48 wherein said first and second promoters are the same.

51. The vector of claim 47, wherein the sense and antisense strands of said RNA molecule are under the control of a single promoter.

52. The vector of claim 51, wherein said single promoter is selected from the group consisting of U6 and H1.

53. A host cell comprising the vector of claim 47.

54. A method of inhibiting replication of hepatitis C virus (HCV) in cells carrying HCV, comprising transfecting said cells with the vector of claim 47.

55. A method of treating hepatitis C in a subject in need thereof, comprising administering a composition comprising the RNA molecule of claim 43 to said subject.

56. A method of treating hepatitis C in a subject in need thereof, comprising administering the vector of claim 47 to said subject.

57. A modified siRNA molecule, comprising a double-stranded RNA molecule of from about 10 to about 30 nucleotides in length, which mediates RNA interference toward a target agent or virus, and which is linked to at least one receptor-binding ligand.

58. The modified siRNA molecule of claim 57, wherein said receptor-binding ligand is attached to a 5' -end or 3' -end of said siRNA molecule.
59. The modified siRNA molecule of claim 58, wherein said receptor binding ligand is attached to multiple ends of said siRNA molecule.
60. The modified siRNA molecule of claim 57, wherein said receptor-binding ligand is selected from the group consisting of a cholesterol, an HBV surface antigen, low-density lipoprotein, an HIV-1 surface antigen, an influenza virus surface antigen, an RSV surface antigen, an HPV surface antigen and a polio virus surface antigen.
61. The modified siRNA molecule of claim 60, wherein said receptor-binding ligand is cholesterol.
62. The modified siRNA molecule of claim 57, further comprising a modification at the 2' position of at least one ribonucleotide, which modification at the 2' position of at least one ribonucleotide renders said siRNA resistant to degradation.
63. The modified siRNA molecule of claim 62, wherein said modification at the 2' position of at least one ribonucleotide is a 2'-fluoro-modification or a 2',2'-fluoro-modification.
64. A method of inducing targeted RNA interference in a patient, comprising administering to said patient an effective amount of the siRNA of claim 57.
65. A method of inducing targeted RNA interference in a patient, comprising administering to said patient an effective amount of the siRNA of claim 61.
66. A method of inducing targeted RNA interference in a patient, comprising administering to said patient an effective amount of the siRNA of claim 63.